

Remarks

Claims 1-32 are pending in the present application, however claims 9-30 are withdrawn as directed to non-elected subject matter. Claims 1-8 and 31-32 have been examined.

Applicants note with appreciation that the rejection of claims 1-8 for indefiniteness for use of the phrase "characterised in that," the rejection of claims 1-3 and 6-8 as anticipated by Ishikura et al., and the rejection of claims 1-8 as obvious over Ishikura et al. in view of Dien et al. have been withdrawn.

Claims 3 and 6 remain rejected as indefinite for use of the phrase "functionally equivalent derivatives." The reason given in the Office Action is that it is not possible to determine what function(s) must be maintained because no specific functions are "disclosed to be engendered" with the objected to phrase.

Applicants have amended claims 3 and 6 to recite language taken from paragraph 32 of the specification as filed. Paragraph 32 describes the functional characteristic of the claimed molecules as relating to the catalytic activity. Paragraph 32 describes variations in the sequence of a DNA molecule or amino acid sequence which do not change the catalytic function of the protein encoded by the DNA molecule or the protein of the amino acid sequence. Because the invention relates to an enzyme, and this enzyme (catalytic) activity is discussed throughout the specification, Applicants submit that the skilled person would understand the terms used in the claims as amended. It therefore would be understandable to the skilled person what is claimed here and the metes and bounds of this invention, particularly in view of the discussion in the specification. Applicants request withdrawal of this rejection.

Claims 4-5 remain rejected as indefinite for use of the phrase "fungal origin." Applicants have amended claim 4 to recite that the reductase is isolated from a fungus as suggested by the examiner. No new matter is added since this isolation is described in the specification. Claim 5 is amended as to form to provide proper antecedent basis in light of the amendment to claim 4. Applicants submit that the rejection has been overcome and consequently request its withdrawal.

Claims 1-4 and 6-8 are rejected as anticipated by Richard et al., FEBS Lett. 457:135-138, 1999 (hereinafter "Richard"). Richard is cited for disclosing an NADH-dependent xylitol dehydrogenase which the Office presumes constitutes a "functionally equivalent derivative" of the enzyme of SEQ ID NO. 2 since it assertedly has the same enzymatic activity. Applicants traverse this rejection.

The Office asserts that the enzyme disclosed in Richard is an L-xylulose reductase, however, this is not the case. Richard discloses a D-xylulose reductase and not an L-xylulose reductase. See, for example, abstract, line 7; page 136, left column, lines 3 and 7-9; page 137, legend to Fig. 3. The enzyme activity clearly is a D-xylulose reductase activity. L-xylulose is not mentioned anywhere in Richard, however D-xylulose is mentioned prominently as the substrate of the enzyme. All sugars in which the enantiomers is mentioned in Richard are D-sugars.

Applicants submit that the skilled person reading Richard would immediately recognize that the subject was a D-xylulose reductase and would know that enzymes acting on D- and L- substrates are not the same or "functionally equivalent." The claims and the art must be read for what the skilled person would understand. Here, skilled persons understand that there is a fundamental difference between an L-xylulose reductase activity

and a D-xylulose reductase activity. There is absolutely no teaching in Richard of any L-xylulose reductase activity, therefore Richard lacks teaching or even a suggestion with respect to this feature of the claims.

The Office deems the enzymes functionally equivalent "in the absence of evidence to the contrary." Office Action, page 4. Applicants submit that Richard itself provides incontrovertible evidence that the enzymes are different and do not have equivalent activity. Further, it is the burden of the Office to demonstrate a clear teaching of each and every element of the claims, not the Applicants' burden to refute unsubstantiated statements that there is teaching. The Office cannot meet its burden with respect to Richard. The anticipation rejection therefore is not proper and must be withdrawn.

Claims 1-8 are rejected as obvious over Richard in view of Dien et al., Appl. Biochem. Biotechnol. 57/78:233-240, 1996 (hereinafter "Dien"). The disclosures of Richard are discussed above. Richard does not teach or suggest any L-xylulose reductase activity. Only D-xylulose reductase activity is mentioned and described. Therefore, Richard does not disclose any activity which could be considered equivalent to the NADH dependent L-xylulose reductase catalytic activity or the enzyme of the claims presented here.

Dien is cited for assertedly teaching that *Ambrosiozyma monospora* can use pentose sugars. Dien, like Richard, does not teach, suggest or even hint at an L-xylulose reductase. Dien describes a D-xylulose activity and an L-arabinose activity. Therefore, even the combination of the references does not result in an L-xylulose reductase activity. One cannot combine these different enzymes to achieve a totally different enzyme, particularly when the activity of the claimed enzyme here is not

even hinted at in the cited art. Thus, the Office cannot meet the first requirement necessary to make out a *prima facie* case of obviousness: the prior art must teach or fairly suggest all elements of the claim.

The Office urges that it would have been obvious to the skilled person to identify the yeast enzymes of Dien using the methods of Ishikura, which is not cited against the claims. This work presumably would involve obtaining the yeast genetic material and guessing the existence of and then isolating the DNA which encodes an NADH-dependent L-xylulose reductase, followed by identification and recombinant production of various enzymes involved in pentose metabolism, mapping out the metabolic pathway and producing recombinants that can economically produce ethanol from hemicellulose biomass. The Office has not even asserted any motivation to perform these numerous and difficult steps or any reasonable expectation of success should they be attempted.

There is no hint whatsoever that an L-xylulose reductase activity even exists, much less in that particular yeast. The Office has not provided any source of specific motivation in the art for the skilled person to modify the teachings of Richard and Dien, which do not even mention L-xylulose, to assume the existence of an NADH-dependent L-xylulose reductase when nothing even points to it. Absent any motivation to discover this enzyme, the Office's case of *prima facie* obviousness fails for this reason as well.

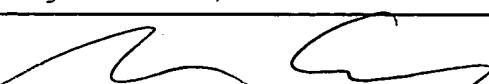
Even if one did hypothesize the existence of the enzyme claimed here, there would be no reasonable expectation of success that the enzyme could be discovered and its DNA isolated as the Office asserts. The Office must point to some reason in the art why a skilled person would reasonably expect successfully

achieving the invention claimed here. The Office has not even mentioned anything which would provide this expectation.

In view of (1) the absence of any teaching or suggestion in the cited art of NADH-dependent L-xylulose reductase activity or enzymes or of any activity which reduces L-xylulose in an NADH-dependent fashion, which could even be considered functionally equivalent by the skilled artisan, (2) the absence of any motivation even to hypothesize the existence of this activity much less go out on a quest to find it, and (3) the absence of a reasonable expectation of success even if one did seek out this activity, the Office cannot make out a *prima facie* case of obviousness against the claims of this application. The rejection should be withdrawn.

The Office has indicated that claims 31-32 are allowable if presented in independent form. Applicants have rewritten these claims in independent form and consequently request their allowance.

Applicants request withdrawal of all objections and allowance of the application at this time.

<b>RESPECTFULLY SUBMITTED,</b>					
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